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10/520,685	05/27/2005	Allan Otto Fog Lihme	036179-0111	9774

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,685	LIHME ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,6-12 and 15-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,6-12 and 15-27* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 4, 2009 has been entered.

Amendment Entry

2. The amendment filed September 4, 2009 has been entered. Claims 2, 7, and 27 have been amended. Claims 1, 3-5, 13-14 and 28 are canceled. Claims 2, 6-12 and 15-27 are under consideration in this office action.

Withdrawal of Objections and Rejections

3. The following objections and rejection are being withdrawn in view of applicants' amendments and arguments:

a) The rejection of claims 2, 4-12, 15, 18-19, 24-25 and 27 under 35 U.S.C. 112, second paragraph;

b) The rejection of claims 2 and 4-12 under 35 U.S.C. 112, second paragraph;

c) The objection of claims 2 and 4-12;

d) The rejection of claims 2, 4-8, 11-12, 15-21 and 24-27 under 35 U.S.C. 102(b) as being anticipated by Zimmerman et al; and

e) The rejection of claims 2, 4-7, 9-10, 16-18, 20-23 and 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Jaber et al.

Response to Arguments

4. Applicant's arguments with respect to claims 2, 6-12 and 15-27 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejection Necessitated by Amendments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2, 6-8, 11-12, 15-21 and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman et al., (US Patent 6,090,292 published July 18, 2000) in view of Flickinger (US Patent 6,036,861 published March 14, 2000).

The claims are drawn to an extracorporeal adsorption method for removing harmful substances responsible of inducing sepsis caused by Gram-negative or Gram-

positive bacteria in a mammal, said method comprising the steps of: a) passing the blood obtained from a mammal through an adsorption column assembly, adapted for fluidized bed adsorption, wherein said adsorption column assembly comprises a column and an adsorption medium in the form of particles, said particles having a density of at least 1.3 g/ml and a mean diameter in the range of 5-1000 um the sedimented volume of said particles being at the most 80% of the volume of the column, said particles being characterized by carrying an affinity specific molecule with a specific affinity for i) the LPS portion of said Gram-negative bacteria and/or ii) Gram-positive bacteria or harmful substances derived from said Gram-positive bacteria, the blood being passed at such a flow rate that a fluidised bed of the particles is formed and b) contacting the harmful substances in the blood to the affinity specific molecules such that the affinity specific molecules bind the harmful substances e) retaining the harmful substances bound to the affinity specific molecules in the column while the blood passes through and exits the column.

Zimmerman et al., teach an extracorporeal adsorption method for removing harmful substances caused by Gram-negative or Gram-positive bacteria in a mammal (col. 2, lines 25-28). Zimmerman et al., teach the method using an adsorption column assembly, comprising a column and an adsorption medium in the form of particles (col. 2, lines 43-48). Zimmerman et al., teach the sedimented volume of said particles being at the most 80% of the volume of the column (col. 3, lines 19-25). Zimmerman et al., teach the having particles carrying an affinity specific molecule with a specific affinity for Gram-negative bacteria wherein the method treats blood by passing the blood through

the adsorption column assembly (col. 2, lines 28-30) at such a flow rate that a fluidized bed of the particles is formed (col. 3, lines 25-32).

Zimmerman et al., teach the adsorption column assembly is adapted for fluidized bed adsorption, in particular stabilized fluidized bed adsorption (col. 4, lines 45-65). Zimmerman et al., teach the mammal being a human being (col. 2, lines 65-68). Zimmerman et al., teach the affinity specific molecule being a peptide, receptor protein, multimeric arrangements or two or more different affinity specific molecules are present on particles within the adsorption medium (col. 3, lines 33-35 and col. 5, lines 35-43). Zimmerman et al., teach the flow rate of the blood through the column assembly is such that expansion ratio of the fluidized bed is at least 1.3 (col. 4, lines 65-68). Thus, Zimmerman teach an arrangement of agitation, buffers and adsorbent particles in which a space between the individual particles wider than the minimum space obtained in a packed column of said particles is achieved, thereby meeting the limitations of a fluidized bed. Zimmerman et al., teach a method wherein a heparin substance is first injected into the blood stream of the mammal (col. 3-4, lines 66-3). While Zimmerman et al., teach using the adsorption column, Zimmerman et al, do not recite particles having a density of at least 1.3 g/ml and a mean diameter in the range of 5-1000 um the sedimented volume of said particles being at the most 80% of the volume of the column particles having a density of at least 1.3 g/ml and a mean diameter in the range of 5-1000 um the sedimented volume of said particles being at the most 80% of the volume of the column.

Flickinger et al., teach protein adsorption by very dense particles in expanded beds. Flinkinger et al., teach column particles having a density of 2.5-3.5. g/ml and a mean diameter in the range of 30-400 um (col. 7, lines 21-23 and 35-38). Flinkinger et al., teach sufficiently dense and of an appropriate particle size for effective fluidization resulting in stable bed expansion; and sufficiently porous for separation of proteins from large volumes of fluids (col. 5-6, lines 55-2). This adsorbent material possesses a significantly high and surprisingly substantially consistent dynamic protein binding capacity when expanded at high fluid velocity, thus, it can be used to adsorb proteins much more rapidly in expanded beds than either inorganic-composite or crosslinked carbohydrate polymeric particles (col. 5, lines 57-64). Furthermore, the expanded bed adsorbent material of the present invention can significantly reduce column cycle time (equilibration, loading to breakthrough, washing, protein elution, cleaning), and cost, in processing large volumes of protein-containing process fluids (col. 5, lines 65-68). Furthermore, there are no detectable particles or fines in the effluent and no detectable clumping of the particles which would cause mixing and nonuniform liquid flow through the bed reducing protein binding capacity (col. 6, lines 1-4).

Therefore it would have been prima facie obvious at the time of applicants invention to modify the extracorporeal adsorption method using fluidized bed adsorption as taught by Zimmerman et al., where the modification incorporates the particles having a density of at least 1.3 g/ml, a diameter in a range of 5-1000um and where the sedimented volume is at most 80% as taught Flickinger et al., in order to provide a significantly high and surprisingly substantially consistent dynamic protein binding

capacity when expanded at high fluid velocity that also rapidly adsorb proteins. No more than routine skill would have been required to incorporate the particles because Zimmerman et al., already teach the use of fluidized beds and Flinkinger et al., teach the advantage associated with the use of very dense particles within the fluidized bed assembly. Furthermore, there is a reasonable expectation of success in incorporating the methods of Zimmerman et al., and Flinkinger et al., since both teach providing fluidized bed assemblies for removing substances using an adsorption column with particles having a density of at least 1.3 g/ml and having affinity specific molecules attached thereto with no change in the respective functions of the particles or the column, thus the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 2, 6-7, 9-10, 16-18, 20-23 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jaber et al., (American Journal of Kidney Diseases. Vol. 30, No 5, Suppl. 4 (November), 1997: pages S44-S56) in view of Flinkinger et al (US Patent 6,036,861 published March 14, 2000).

The claims are drawn to an extracorporeal adsorption method for removing harmful substances responsible of inducing sepsis caused by Gram-negative bacteria in a mammal, wherein said method comprises treating blood obtained from said mammal by passing the blood through an adsorption column assembly at such a flow rate that a fluidized bed of the particles is formed and the harmful substances are removed from the blood by binding of the harmful substances to the affinity specific molecules, thereby retaining them in the column, and wherein said adsorption column assembly comprises a column and an adsorption medium in the form of particles, the sedimented volume of said particles being at the most 80% of the volume of the column, said particles being characterized by carrying an affinity specific molecule with a specific affinity for the LPS portion of said Gram-negative bacteria, and/or ii) Gram-positive bacteria or harmful substances derived from said Gram-positive bacteria.

Jaber et al., teach extracorporeal adsorption method for treating gram-negative bacterial sepsis. Jaber et al., teach adsorbent-based blood purification founded upon adsorption, which removes harmful molecules by binding those molecules onto the surface of a material (page S44, col.2). Jaber et al., teach specific affinity molecules being antibodies coated onto micro spheres (page S53, col.1). See Table 1. Jaber et al., teach that polymyxinB has affinity for the Lipid A moiety of LPS from gram-negative bacteria (page S48, col. 2). Jaber et al., teach polymyxin B-Immobilized onto Sepharose bead with an affinity solid-phase column for the selective on-line removal of endotoxins during plasmapheresis (page S52, col. 1). Jaber et al., teaches using the affinity column device on rats in an on-line plasmapheresis with PMX-B sepharose beads having a

diameter of 0.1 to 5um (page S52, col.1). Jaber et al., teach the endotoxin clearance rate was excellent (page S52, col.1). Jaber et al., also teach the use of polymyxin B-Immobilized macroporous cellulosic beads having a diameters of 60 to 80um, showing a more than 99.5% removal of endotoxins (page S52, col.1) Jaber et al., teach a flow rate of 200ml/min (page S53, col.1). Jaber et al., teach hemoperfusion methods wherein the flow rate was 80-100ml/min (page S50, col.2). Jaber et al., teach treating human whole blood or human plasma containing herapin or an anticoagulant on columns (page S49 col.2). However Jaber et al, do not recite particles having a density of at least 1.3 g/ml and a mean diameter in the range of 5-1000 um the sedimented volume of said particles being at the most 80% of the volume of the column particles having a density of at least 1.3 g/ml and a mean diameter in the range of 5-1000 um the sedimented volume of said particles being at the most 80% of the volume of the column.

As discussed above, Flinkinger et al., teach et al, particles having a density of at least 1.3 g/ml and a mean diameter in the range of 5-1000 um the sedimented volume of said particles being at the most 80% of the volume of the column particles having a density of at least 1.3 g/ml and a mean diameter in the range of 5-1000 um the sedimented volume of said particles being at the most 80% of the volume of the column.

Therefore it would have been prima facie obvious at the time of applicants invention to modify the extracorporeal adsorption method using fluidized bed adsorption as taught by Jaber et al., where the modification incorporates the high density particles having a density of at least 1.3 g/ml, a diameter in a range of 5-1000um and where the sedimented volume is at most 80% as taught Flickinger et al., in order to provide a

significantly high and surprisingly substantially consistent dynamic protein binding capacity when expanded at high fluid velocity that also rapidly adsorb proteins without the problems associated with Sepharose beads. No more than routine skill would have been required to incorporate the high density particles because Jaber et al., already teach the use of fluidized beds, adsorption column and particle while Flinkinger et al., teach the advantage associated with the use of very dense particles within the fluidized bed assembly. Furthermore, there is a reasonable expectation of success in incorporating the methods of Jaber et al., and Flinkinger et al., since both teach providing fluidized bed assemblies for removing substances using an adsorption column with particles and Flinkinger et al., teach the benefits of incorporating high density particles of at least 1.3 g/ml, having affinity specific molecules attached thereto with no change in the respective functions of the particles or the column, thus the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

New Grounds of Objection Necessitated by Amendments

Claim Objections

7. Claim 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Dependent claim 18 is drawn to the particles having a density of at least 1.3g/ml and a mean diameter in the

range of 5-1000um; however claim 27 already recites the particles having a density of at least 1.3g/ml and a mean diameter in the range of 5-1000um. Therefore clarification is required to overcome the objection.

Conclusion

8. No claims allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/
Primary Examiner, Art Unit 1645